901-14 Regional Variation in Angioplasty Practice in the United States: A Report From the Hirulog Angioplasty Study

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The diagnosis of unstable angina (UA) comprises various clinical features having a wide range of risk for adverse outcomes. Geographic variations in cardiac treatment exist in the U.S., but variations in the use of PTCA for UA have not been reported. 3641 of 4098 patients (89%) enrolled in the Hirulog Angioplasty Study were from U.S. census regions: (1) New England, (2) Mid-Atlantic, (3) South Atlantic, (4) East Central, (5) West Central, and (6) West. All patients undergoing PTCA had UA (new-onset, crescendo or rest pain), but the proportion of patients undergoing PTCA for high-risk clinical features, or for only mild lesions (< 50% by quantitative angiography) varied sharply across regions:

Region	1	2	3	4	5	6	P
n	467	581	1026	576	551	440	
Post-MI (%)	24.2	17.2	18.2	13.5	20.6	16.1	0.001
Rest pain (%)	77.9	59.7	67.3	50.9	64.6	59.8	< 0.001
Prior heparin (%)	50.9	35.6	42.3	32.3	35.9	39.4	< 0.001
Mild lesions (%)	4.3	7.1	8.2	6.4	7.1	4.3	0.03
Maj. Comps (%)	3.4	3.1	4.9	5.6	4.4	6.7	0.07

Thus, patients in New England have more rest pain, more post-MI angina, and fewer lesions of debatable significance. Nevertheless, these higher-risk patients have the same rate of complications (death, MI, CABG) as those in other regions. The relation between the use of PTCA for UA and clinical outcomes requires urgent study.

ANGIOPLASTY – RESTENOSIS – BASIC

901-15 Endovascular Radiation Reduces Vascular Lesion Formation (VLF) After Balloon Injury (BI) of Pig Coronary Arteries by Inhibiting Cell Proliferation

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Ionizing radiation (IR) has been shown to reduce (VLF) following (BI) of pig coronary arteries. To determine the mechanism by which IR reduces VLF, BI was performed on the LAD, LCX, and RCA arteries of 22 pigs. Immediately following BI, a flexible catheter with a pure beta emitter 90 SR/Y was introduced to deliver 14 or 28 Gy (to a depth of 2 mm) into 14 of the injured arteries. Animals were killed 3 and 7 days after injury. 5-Bromo-2-deoxyuridine (Brdu) was administered 24 hours before sacrifice to label the proliferating cells. Immunohistochemistry was performed on frozen sections with monoclonal antibodies to Brdu and the number of Brdu positive cells relative to the total number of cells was determined using computer-based image analysis. Cell proliferation was significantly reduced by 3 days after BI in the media and adventitia of irradiated vessels. There was no evidence of cell death and necrosis in arteries exposed to IR. Alpha actin staining used as an index of vascular remodeling appear to be lower in the adventitia of the irradiated vessels.

% of Brdu	Control		14 Gy		28 Gy	
Labeling	3 days	7 days	3 days	7 days	3 days	7 days
Adventitia	28.1	9.6	18.6*	8.0	7.1**	3.4
Media	14.4	4.6	7.6*	5.3	8.1	8.2

*p = 0.04 versus control 3 days, **p < 0.0003 versus control 3 days

Conclusions: These studies suggest that endovascular radiation reduces VLF by inhibiting the first wave of cell proliferation in the adventitia and the media.

901-16 Tissue Factor Pathway Inhibitor Attenuates Prothrombinase Complex Formation on Balloon-Injured Arteries in Pigs

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We have shown that intravenous infusion of tissue factor pathway inhibitor (TFPI), the physiologic inhibitor of factor Xa and tissue factor/factor VIIa, essentially abolishes stenosis measured 4 wk after balloon-induced carotid arterial injury in minipigs. To determine whether the effect of TFPI on stenosis is associated with early decreases in procoagulant activity and thrombosis on the luminal surface, we injured both carotid arteries by balloon hyperinflations in 27 anesthetized pigs given either TFPI (0.5 mg/kg bolus and 100 μg/kg/min, i.v., n = 10) or heparin (200 U/kg bolus and 100 U/kg/h, n = 17) as a control for 24 h. Indium-111-labeled autologous platelets were injected 1 h before collection of the arteries within 24 h for measurement of thrombosis. Injured arterial segments were incubated with chromogenic substrate for assay of factor Xa (S2222) and perfused with recalcified human plasma for assay of fibrinopeptide A (FPA) in the eluant to measure the rate of thrombin-mediated fibrin formation. Platelet deposition trended to be higher on arteries from animals given TFPI compared to those given heparin (p = 0.06). However, factor Xa activity was 4-fold lower on TFPI-treated arteries compared with heparin-treated arteries (p = 0.012). In addition, FPA generation in the eluant after 10 min was reduced on TFPI-treated (222 ± 72 (SE) ng/ml) compared with heparin-treated arteries (1503 ± 376 ng/ml, p = 0.004). Thus, while platelet deposition was not attenuated, prothrombinase complex and the resulting procoagulant activity of the luminal surface were diminished substantially by TFPI. We conclude that promising results with TFPI in the porcine angioplasty model likely result from decreased local thrombin generation.

ANGIOPLASTY – RESTENOSIS – CLINICAL

901-17 Endovascular Low Dose Radiation for Prevention of Restenosis Following Angioplasty for Treatment of Narrowed Dialysis Arterio Venous Grafts

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Failure of arterio-venous grafts (AVG) of chronic dialysis patients remains a problem despite repeated balloon angioplasty (PTA). The purpose of this study was to determine whether low dose intravascular radiation therapy following PTA will retard neointimal hyperplasia in patients who have failed conventional balloon PTA for stenosis at the AVG. Eleven patients underwent PTA to 14 narrowed (> 50% luminal stenosis) dialysis AVG sites. After obtaining a good angiographic result and reduction of pressure gradient a delivery catheter was placed at the angioplasty site, and intravascular radiation was calibrated to a dose of 14 Gy at a depth of 2 mm to the arterial wall. The patient was then treated with a high activity ^{192}Iridium line source delivered to the treatment site by a high dose rate afterloader. All patients treated had good angiographic results post angioplasty and successful delivery of the radiation treatment into the AVG without complications. During mean follow-up of 164 ± 36 days at monthly intervals, ultrasound revealed patent and functioning AVG for dialysis in 13 out of 14 grafts. One patient had graft thrombosis three months after the procedure. *Conclusions:* Intravascular radiation following balloon angioplasty to narrowed AVG in chronic dialysis patients is feasible and may reduce the restenosis rate and extend the survival of these grafts.

901-18 Local Drug Delivery of Low Molecular Weight Heparin After PTCA: First Clinical Experience Using the Porous Balloon (PILOT-Study)

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Aim of this trial was to assess the safety and efficacy of local drug delivery (LDD) of low molecular weight heparin Reviparin (Knoll Inc., Ludwigshafen, Germany) using a porous balloon to prevent restenosis after PTCA.

The 2.7 mm porous balloon (SI III, ACS, CA, USA) used in this study had 35 holes in a spiral pattern (hole diameter of 75 μm). Fifteen patients (male n = 9, female n = 6, age 61 ± 8 years) undergoing successful PTCA (LAD n = 10, RCX n = 3, RCA n = 2) were treated locally with Reviparin (1500 anti-Xa-units/4 ml, 2 atm) and during the following 24 hours with additional 10500 anti-Xa-units Reviparin intravenously. For the following 28 days the patients received further 7000 anti-Xa-units Reviparin subcutaneously. Angiograms were obtained before and after PTCA, after LDD and after 24 hours.

The primary device success rate was 100%. Quantitative coronary angiography showed a minimal luminal diameter of 0.43 ± 0.08 mm before PTCA, 1.79 ± 0.29 mm after PTCA, 1.57 ± 0.25 mm after LDD and 1.59 ± 0.30 mm after 24 hours. No major complication (e.g. myocardial infarction, bleeding complications, bypass surgery or death) occurred during the 28 days follow-up-period.

Conclusion: The initial results of this ongoing trial suggest, that local drug delivery with low molecular weight heparin using the porous balloon after PTCA is feasible and safe. Data on restenosis will be available at the 6 months angiographic and clinical follow up.